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FDA Regulatory Failures in Enforcing Limits on GLP-1 Compounding Puts Patients at Risk: How to protect and advance the public health through more robust regulatory oversight and timely legislative action

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Abstract

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In recent years, U.S. Food and Drug Administration (FDA)-approved GLP-1 medicines have surged in popularity as treatments for diabetes and obesity. A temporary shortage of these drugs opened the door to a flood of unapproved knockoffs from compounding pharmacies looking to cash in. The shortage has ended, but some compounders continue to mass produce compounded knockoffs, which ignores longstanding limits on compounding and puts patients at risk.

Unlike FDA-approved drugs manufactured under strict standards, compounded drugs are not subject to FDA approval and are never reviewed by the Agency for safety, efficacy, or quality. Regulators and public health experts have repeatedly warned that compounded drugs carry unique, heightened safety risks and should not be used when FDA-approved drugs are available. Compounding was intended as a narrow exception-for patients whose needs can't be met by approved drugs-not for mass-producing untested products.

The rise of large-scale compounding of GLP-1 drugs raises grave concerns. And those concerns are magnified by compounders' disregard for the law. Even after the FDA made clear that mass compounding of semaglutide (Ozempic, Wegovy) and tirzepatide (Mounjaro, Zepbound) must stop, some compounders continue to manufacture and sell these unapproved products. Lax enforcement of longstanding legal limits on compounding has allowed this dangerous practice to persist-endangering patients and threatening another preventable public health crisis.

This report outlines the critical role of FDA's drug approval system in protecting patients and underscores how enforcement failures undermine drug safety and regulatory integrity.

It begins with an overview of the U.S. regulatory framework-specifically the FDA approval process, which ensures drugs are safe and effective, and the limited compounding exception designed for individualized patient care and then turns to how enforcement gaps are enabling unlawful compounding, focusing on three key areas:

1. Bogus personalization schemes used to disguise mass production;

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2. Use of dangerous, unregulated foreign ingredients; and

3. False advertising that misleads patients about safety and efficacy.

This report also includes recommendations for Congress and the FDA to crack down on these illegal practices.

History makes clear that unchecked compounding can lead to public health disasters. With GLP-1 drugs, the warning signs are flashing-and the law already provides tools to act. What's needed now is the will to enforce them before it's too late.

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1. FDA Approval System: The Gold Standard For Safety and Quality

For decades, the FDA approval process has served as the lynchpin to ensuring safe and effective medicines are available for patients. Patients can trust that FDA-approved medicines meet the highest standards for safety and efficacy. Compounding-creating a custom drug for an individual patient-is a narrow exception to the FDA approval system. However, there are carefully drawn limits on compounding activity, intended to ensure that compounding does not become a backdoor for unregulated mass manufacture of drugs.

1a. Background on FDA Approval System

Congress passed the Food, Drug, and Cosmetic Act (FDCA) in 1938, creating a robust regulatory framework that would help ensure that the medicines Americans take are safe and effective.

The centerpiece of this system is the New Drug Approval (NDA) process through which new pharmaceutical drugs must be reviewed and approved by the FDA. The FDA approval system is globally recognized as the gold standard for safe medicine.

To obtain FDA approval, an applicant must meet several rigorous requirements. In particular, the applicant must show that:[1]

- Double-blind, placebo-controlled trials demonstrate that the drug is safe and effective in its proposed use and that the benefits of the drug outweigh the risks;

- The drug's proposed labeling (package insert) is accurate and includes appropriate instructions for use, recommended dosing, and other important safety information; and

- The methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity.

FDA approval is difficult to obtain-around 90% of drug candidates ultimately fail.[2] This is a long-standing feature of a quality approval process, not a flaw. The rigors of the FDA approval process are intended to ensure that the medicines Americans take are held to the highest standards of safety and quality.

FDA-approved drugs also must comply with a comprehensive and complementary set of safety requirements for drug manufacturers, including:

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- Disclosure of every step, ingredient, and component in the manufacturing process to the FDA;

- Registration and inspection of facilities;

- Adherence to Current Good Manufacturing Practices (cGMP); and

- Ongoing pharmacovigilance and reporting of adverse events.

In addition to regulating name-brand prescription drugs, FDA also oversees generic drugs. While the approval process for generic drugs is not the same as that for newly-developed, brand-name drugs, generic drugs must still be approved by the FDA-that means they must still meet FDA's strict standards for safety, quality, and efficacy.

1b. Compounding: A Narrow Exception-Not a Broad Exemption-to the FDA Approval System

Compounding is generally defined as the process in which a pharmacist creates a custom drug tailored to a specific patient's unique medical needs. This is how most medicines were created in early American history. As industrialization and mass manufacturing techniques provided safer, more effective ways to produce drugs at scale, compounding's function in the drug supply chain rightly contracted to a much more limited, though important role serving patients whose needs cannot be met by commercially available medicines. For example, if a patient has an allergy to a dye or other ingredient in the commercially available FDA-approved medicine, a pharmacy can "compound" a custom version for that patient without the dye.

Notably, compounding is not the same as producing a generic version of a drug. Generics may be (and usually are) mass-produced. But compounding is the creation of a custom version of a drug for a specific patient.

Congress recognized that compounding pharmacies can serve a valuable role for specific patients with unique medical needs that cannot be met by mass-manufactured medicines. Congress also recognized that it would be impractical to require pharmacies to go through the FDA approval process each time they were asked to compound a medicine specially tailored to the needs of a unique, individual patient. Thus, compounding pharmacies are not regulated like drug manufacturers. Their products are not subject to FDA approval and, as a result, they "can be risky for patients."[3]

Because of this minimal oversight and resulting risks to patient safety, Congress has for decades drawn careful limits on the scope of permissible compounding to prevent it from becoming a backdoor for unregulated mass manufacturing of drugs. Indeed, as early as 1962, Congress made clear that compounding is permitted only in "the regular course of [a pharmacy's] business of dispensing or selling drugs or devices at retail."[4] To produce drugs at scale requires registration and treatment as a drug manufacturer.

Federal law permits compounding by two different types of entities: 503A compounding pharmacies and 503B outsourcing facilities.[5] Historically, most compounded GLP-1 products have been made by 503A compounding pharmacies, and now that FDA has resolved the semaglutide and tirzepatide shortages, 503B outsourcing facilities are no longer permitted to make any compounded semaglutide or tirzepatide medicines.

503A compounding pharmacies

503A facilities are exempt from many key FDA requirements, including:

- FDA approval under the NDA process;

- FDA registration and product listing;

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- adherence to cGMP;

- labeling and instruction for use requirements; and

- pharmacovigilance and adverse event reporting.[6]

Because of the minimal regulatory oversight 503A compounding pharmacies face, the law imposes strict limits on the circumstances in which they can compound drugs.

First, 503A pharmacies may compound only for an "identified individual patient," and they are prohibited from producing products that are "essentially a copy" of any "commercially available" medicine.[7] In guidance documents, the FDA has indicated that it interprets "commercially available" to mean any medicine that is not on its drug shortage list.[8] These strict limitations were intended to allow compounding in narrow instances while "limiting the scope of compounding so as to prevent manufacturing under the guise of compounding."[9]

Federal law also imposes limits on 503A compounders broadly distributing their products across the country. Specifically, 503A facilities are prohibited from shipping more than 5% of the compounded drugs they make outside the state in which they operate unless the state enters into a memorandum of understanding ("MOU") with FDA to ensure adequate oversight by state regulators.[10] The logic behind this rule is straightforward: It helps prevent mass distribution of potentially unsafe drugs and makes it easier to identify the source of unsafe compounded drugs in the absence of adverse event reporting and pharmacovigilance requirements.

This 5% requirement has not been enforced since its inception in 1997. In response to legal challenges by compounders, the FDA has maintained a policy that it will not enforce the requirement until it finalizes a "standard" MOU for states to consider.[11] Every time FDA gets close to finalizing a standard MOU, the compounders sue to invalidate it.

503B outsourcing facilities

503B facilities are subject to slightly different rules than 503A compounders. Section 503B permits production of compounded drugs in bulk (i.e., without a prescription for a specific patient), but only in two circumstances: (a) when the drug uses bulk drug substances for which there is a "clinical need" as identified by the FDA, or (b) when there is a shortage of the drug as determined by the FDA.[12] GLP-1s are not on the clinical needs list and, as of earlier this year and late last year, neither semaglutide nor tirzepatide are in FDA-declared shortage.

Because it provides for bulk production of drugs, Section 503B imposes some additional guardrails beyond 503A. For example, outsourcing facilities must (a) register with the FDA and permit inspections, (b) report the compounded drugs they produce, and (c) follow cGMP.[13]

However, 503B outsourcing facilities still exempt from many requirements facing conventional drug manufacturers,[14] and they are rarely inspected by FDA or other regulators. But when they are inspected, FDA usually has "significant objectionable observations." And 503B, like 503A, was never intended to open the door to a means of mass manufacturing unapproved drugs when FDA- approved drugs are available to meet patient needs. Thus, outsourcing facilities still cannot make "essentially a copy" of any FDA-approved drugs unless the drug is in shortage.[15]

2. Failures in Enforcing The Limits on Compounders Puts Patients At Risk

Compounded drugs are untested, unproven, and subject to minimal oversight. Patient injuries and even deaths have been an all-too-common consequence of

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unsafe compounding practices. The strict limitations that Congress has imposed on the production of compounded drugs reflects their heightened risks-compounded drugs are supposed to be a tailored solution for individuals with unique needs, not a substitute for FDA-approved drugs.

Indeed, if a patient genuinely needs a compounded drug because the commercially available, approved drug contains an ingredient that would lead to anaphylactic shock, then the choice is simple-the patient either takes a compounded drug, despite the risk, or they take no drug at all. Faced with that choice, the risk-reward balances in favor of compounding. But the calculus is entirely different when a perfectly suitable FDA-approved medicine is commercially available.

There has been an alarming rise in schemes from compounders trying to end-run these limitations, from using phony "personalization" of drugs to relying on illicit foreign ingredients to misleading patients about their products. Compounding is not-and has never been intended to be used as

a backdoor for mass manufacturing of prescription drugs with virtually no FDA oversight. If left unchecked, these schemes threaten to create an unprecedented and entirely preventable disaster.

2a. Background on Safety Risks of Compounding

The NECC Disaster. The 2012 New England Compounding Center (NECC) tragedy highlights the life-threatening risks of inadequate oversight of compounders.[16] NECC, a Massachusetts-based compounding pharmacy, sold a compounded injectable drug contaminated with fungal meningitis,resulting in the largest public health crisis caused by a contaminated pharmaceutical drug in American history. Ultimately, NECC's contaminated injectable products sickening at least 750 people across at least 20 different states. More than 100 Americans died as a result of the infected products.

The NECC tragedy was a wake-up call for patients, advocates, and regulators. Multiple executives were criminally prosecuted, and in response to the NECC outbreak, Congress passed the Drug Safety and Quality Act of 2013, adding Sections 503A and 503B to reaffirm the strict limitations on compounding.[17] Unfortunately, many of those laws have not been enforced by FDA, leaving the country at risk for another serious tragedy.

History of Safety Problems. While the NECC incident is the most shocking illustration of compounding's risks, it is far from the only one. A report from the Pew Charitable Trusts that studied illnesses and deaths associated with compounded drugs from 2001 to 2019, found dozens of other examples both before and after NECC:[18]

- For instance, in 2017, dozens of patients developed septic arthritis after using an injectable drug from a New Jersey compounder that was contaminated with bacteria.

- Similarly, in 2011, nineteen people in Alabama were sickened, including nine who were killed, after taking a contaminated parenteral drug that led to a bacterial bloodstream infection.

- In 2007, a Texas compounder sold an injectable product that was eight times stronger than the labeled concentration, causing overdoses that killed three people.

- And in 2001, a California compounder's contaminated joint injection product caused several adverse events-from meningitis to abscesses to an infected hip-that killed three people and sickened ten others.

Pew's findings also revealed that of the 43 states examined, only 13 required compounders to report serious adverse events. The report concluded that

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"[because many such events go unreported," its analysis was "an underestimation" of the number of adverse events caused by compounded products.

Given this history, the FDA has repeatedly warned about the safety risks of compounding. The FDA has cautioned that compounded products are "risky for patients" and that "poor compounding practices can result in serious drug quality problems" that "can lead to serious patient injury and death."[19]

Recent Issues with GLP-1 Compounders. There are numerous examples of safety issues with compounded drug products, including compounded GLP-1s. For instance, recent media investigations into Empower Pharmacy, which touts itself as America's "largest and most advanced" compounding pharmacy, revealed a decade-long pattern of safety issues, punctuated by multiple FDA warning letters that Empower had "put patients at risk" through its "[r]epeated failures" to use safe manufacturing practices.[20] Other inspections revealed serious concerns about Empower's ingredients, including some instances where "food grade" ingredients were used, which are not purified to pharmaceutical grade and are more likely to be contaminated. Given these issues, it's no surprise that Empower recently recalled over 8,000 vials of testosterone due to concerns over their sterility.[21]

Similarly, in November 2024, the FDA issued a warning about unsafe compounding practices at Fullerton Wellness, a California compounder of GLP-1 drugs.[22] The FDA cautioned that Fullerton Wellness "used non-sterile ingredients" and "took no steps to sterilize them," putting patients at risk of "serious and potentially life-threatening adverse health consequences including infections and sepsis."

Safety concerns like these translate into real-world harm for patients. While the lack of pharmacovigilance for compounded drugs makes it difficult to know the extent of the problem, the evidence is mounting that lax standards by mass compounders of GLP-1 drugs is threatening another NECC tragedy. Researchers at Binghamton University who studied the limited set of adverse events that have been reported for compounded GLP-1s found that they were nearly 2.5 times likely to result in hospitalization compared to FDA-approved GLP-1 medicines.[23]

There are also alarming reports of dosing errors and overdoses. Patients taking compounded GLP-1 drugs have reported accidental overdoses caused by confusing labeling and lack of instructions for use.[24] These overdoses have led to many serious adverse events-in some cases requiring hospitalization. America's Poison Control Centers noted that in 2023, calls about accidental overdoses of GLP-1s had spiked by over 1,500% compared to 2019, and independent tests of compounded GLP-1s by media outlets have revealed products with 250% of the listed potency, creating a serious overdose risk.[25] And again, because there are minimal requirements on compounders to report adverse events, the few stories of patient safety problems in public media reports are likely just the tip of the iceberg.

2b. Phony "Personalization" Schemes: An Unlawful and Dangerous Experiment on Unsuspecting Patients

Policymakers have responded to the pattern of compounded drug health crises by repeatedly imposing strict limits on permissible compounding activity. Chief among these is the prohibition on compounders producing drugs that are "essentially a copy" of any "commercially available" medicine.[26]

In recent years, the tremendous demand for semaglutide and tirzepatide led to shortages of both drugs. During this shortage, the number of compounding pharmacies making copies of GLP-1 drugs exploded, with such entities producing and distributing the drugs in mass quantities. That shortage is now over. The FDA removed both semaglutide and tirzepatide from its shortage list after confirming that FDA-approved versions of both drugs are available in sufficient quantities to meet patient demand. That should have been the end of mass compounding.

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But it was not. Instead, compounders unsuccessfully filed lawsuits seeking to challenge the FDA's finding that the semaglutide and tirzepatide shortages are over.[27] Accordingly, because FDA-approved versions of semaglutide and tirzepatide are "commercially available," the FDA has confirmed that mass compounding of these drugs must stop.[28]

While some compounders have stopped selling compounded GLP-1s to comply with the law, others are using a so-called "personalization" scheme to try and continue selling mass-manufactured compounded GLP-1s. These compounders are intentionally manipulating their products, claiming that they are making "personalized" medicine that therefore is not "essentially a copy" of FDA-approved semaglutide or tirzepatide. For example, some compounders are selling oral versions of GLP-1s, even though the FDA has only approved semaglutide and tirzepatide in injectable form.

Others offer compounded semaglutide and tirzepatide with altered doses that differ from the FDA- approved dosage amounts. And some compounders are selling compounded GLP-1s with an additive in the product, like a vitamin or glycine.

Such phony "personalization" schemes not only ignore the language of the FDCA, a federal statute, they are dangerous. There is nothing "personalized" about these mass-produced products. It appears that compounders are simply making the same change across the board for all patients with no "personalization" whatsoever-this is nothing but a pretext for compounders to claim that they are not making "essentially a copy" of the FDA-approved drugs. But under Section 503A, making a drug that is not "essentially a copy" means making some alteration that makes a "significant difference" for the specific patient for whom it is compounded.[29] There is no evidence these changes will make any difference and certainly not "a significant difference" for patients, let alone all of them *en* masse. Indeed, some compounders have even admitted as much, marketing their manipulated products by claiming that they are no different from FDA-approved versions or that the changes are so minor that they would not have a clinically significant effect.

Selling these unapproved drugs with untested alterations or combinations is effectively a mass experiment on unsuspecting patients-a clear and present danger to public health. Our system is not supposed to work this way. Compounding was simply never intended to provide an alternative pathway for the mass manufacture of unapproved prescription drugs with minimal regulation or oversight. And the FDCA was certainly never intended to facilitate mass distribution of untested new drugs such as the phony "personalized" products being marketed by some today. Failing to put a stop to these fake "personalization" schemes doesn't just endanger the patients who take them, it threatens to undermine public trust in our nation's ability to supply patients with safe medicines.

2c. Compounded GLP-1s Rely on Dangerous and Illegal Foreign Suppliers

The safety risks from continued mass compounding of GLP-1s are heightened because compounded GLP-1s rely on a supply of active pharmaceutical ingredients (API) from dangerous and illegal foreign sources.

Federal law demands that API used in any product sold in the U.S., including compounded drugs, can only come from entities that are properly registered with the FDA. If the entity is not registered, under federal law, the FDA is required to refuse entry of the shipment.[30]

Yet publicly available data shows that most of the API imported into the U.S. by entities other than Novo Nordisk and Eli Lilly and Company, the makers of FDA-approved semaglutide and tirzepatide products, is from entities that are either not registered with the FDA or have never once been inspected by the FDA to ensure compliance with cGMP and other safety requirements. Indeed, even though the law

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mandates the rejection of shipments from unregistered facilities, reports indicate that over 80% of unregistered shipments are allowed into the country.[31]

An analysis from the Brookings Institution detailed that the vast majority of these foreign API shipments come from China.[32] These facilities typically have never been inspected for safety or quality by anyone-not FDA and not even Chinese authorities. In many cases, their products cannot even legally be sold in China because the country imposes strict domestic standards on ingredients for medicines to be sold. But those standards do not apply if the ingredients are made solely for export to the United States. This "good enough for America" policy undermines American interest in ensuring public health and safe pharmaceutical supply chains, and it should not be tolerated.[33]

The limitations on foreign API importation are not simply bureaucratic red tape; but a broader failure of enforcement and oversight that is causing very real safety risks. For example:

- Customs data shows that some of these shipments contain "research only" API, meaning that the product has not been purified to pharmaceutical grade.[34] "Research only" products are not safe for human use, and no one should take them. Yet, as the FDA and other regulators have warned, some entities are putting patients in danger by selling knock-off GLP-1s made from these "research only" ingredients.[35]

- Other shipments contained GLP-1 API that was not sterile, or that was marked for use in an untested and unapproved product form, such as an ointment.[36] Some shipments suggested the API was for use in prescriptions for animals. There are, however, no approved uses of GLP-1s in animals, underscoring that those shipments were fraudulent.

- Similarly, illicit foreign API helps fuel the sale of counterfeit GLP-1 products. Law enforcement and advocacy groups have seen a rise in counterfeit schemes intended to deceive patients into believing that they are getting genuine, FDA-approved GLP-1 medicine, when in fact, they're taking a dangerous and illegal knock-off.[37]

These issues are even more glaring because they should never be happening in the first place. Multiple legislators have put a spotlight on illicit foreign API in recent months. For example, Senators Jim Banks of Indiana and Thom Tillis of North Carolina have both sent letters to the FDA expressing their concern over "the proliferation of injectable weight-loss drugs compounded using tainted APIs imported from China, India, and other countries" and calling on the agency to do more to address "the growing public health threat posed by counterfeit and illegally imported GLP-1[s]."[38] The FDA must step up enforcement of the laws already on the books to put a stop to these dangers.

2d. False and Misleading Marketing Deceives Patients About the Risks

The risks from compounded GLP-1s are especially serious because patients are often misled about them. Most concerning is outright counterfeiting, where sellers illegally try to pass their products off as genuine, FDA-approved medicine. But even when not blatantly counterfeit, there are still systemic problems with marketing and advertising for compounded products.

A January 2025 study found that websites that sell compounded GLP-1s products often offered only half-truths and sometimes entirely misinformed potential consumers.[39] Most websites did not disclose that compounded GLP-1 products are not FDA-approved, and some even falsely suggested that their products were FDA-approved or were "generics." Other websites provided limited safety information and made misleading efficacy claims.

Similarly, a recent survey of women conducted by National Consumers League

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found that 71% of respondents incorrectly believed that compounded drugs must be tested and proven safe to be on the market, pointing to a "tsunami" of mostly misleading or false advertising and promotional content.[40]

As with illicit foreign API, policymakers have raised concerns about this issue. Earlier this year, Senators Dick Durbin and Roger Marshall sent a bipartisan letter to FDA expressing their concern about a misleading advertisement for compounded drugs, omitting any safety or side effect information, that aired during the Super Bowl-the most widely-viewed television event in the country.[41]

The dangers from inadequate oversight of compounded drugs are cause for alarm by themselves-all the more so when patients are unaware of those dangers due to misleading marketing.

3. Calls To Action to Protect American Patients

FDA must put a stop to phony "personalization." The FDA must make clear that compounders cannot mass produce manipulated GLP-1 drugs under the false pretense of "personalization." Simply adding an ingredient to semaglutide or tirzepatide *en masse* or changing doses or routes of administration for swaths of patients is not personalization, and it does not create a significant difference for anyone. If FDA fails to put a stop to this practice, it will create an alternative, virtually unregulated pharmaceutical market that operates outside the safeguards and consumer protections provided by the FDCA.

FDA must require compounding pharmacies who act like drug manufacturers to register as drug manufacturers. Again, this requires nothing more than carrying out the law as it is written. FDA should require compounders to register as drug manufacturers if they produce drugs "other than in the regular course of their business" of dispensing or selling drugs at retail.[42] If compounders manufacture drugs at scale, they should be treated like drug manufacturers, plain and simple.

FDA and Customs Border Control (CBP) must enforce restrictions on illicit foreign API. Federal law already requires rejection of API shipments from unregistered foreign entities or that contain API that could not legally be used in products sold to patients in its country of origin. Enforcing this law will put a stop to all kinds of illicit foreign product-from dangerous "research only" API to potentially unsafe ingredients that counterfeiters rely on. As both a matter of law and patient safety, FDA and CBP can no longer neglect their obligations to our drug supply chain safe.

Congress must require the FDA to enforce the 5% rule. FDA's decision not to enforce the 5% rule turns the law on its head. Section 503A explicitly prohibits inter-state distribution of more than 5% of a compounder's products unless and until the state enters an MOU with FDA. Instead of doing that, FDA has declined to enforce the 5% rule until an MOU is finalized- the opposite of what Congress intended. Enforcing the 5% rule as Congress intended will help prevent another NECC disaster in which an unscrupulous compounder in one state can endanger patients across the country.

Congress must increase FDA resources to enforce the law as it stands. It is clear from the above that existing law already provides a solution to many of these problems. But enforcing the law requires resources, and Congress must give the FDA the resources it needs to do the job.

Failure to act risks eroding trust in our healthcare system generally. For decades, Americans have relied on the robust regulatory system in place to ensure that the medicines they take are safe and effective. If unscrupulous actors are allowed to continue putting patients at risk by exploiting regulatory lapses, it undermines trust in the whole system. The time to act is now.

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4. Conclusion

The GLP-1 shortage is over, but the illegal, unsafe, and venal exploitation of the American public by mass-scale "corporate" compounders masquerading as pharmaceutical companies continues.

Corporate compounding pharmacies are illegal and unregulated pharmaceutical companies. The safety and effectiveness of their drugs are not tested by the FDA, their manufacturing facilities are not inspected, and they do not report adverse events to the agency. "Buyer beware" is not smart or acceptable healthcare policy. No one should be playing Russian Roulette-or Chinese Checkers- with unapproved, untested, or unregulated drugs. Corporate compounding of GLP-1 medicines is a growing part of the misinformation crisis facing the FDA. Attention must be paid.

Relative to the ubiquitous advertising and promotion of compounded GLP-1 products, why hasn't there been more aggressive regulatory action? Currently, the FDA only targets false or misleading posts by influencers or corporate compounding companies when they have an established financial relationship with the legitimate manufacturer of the drug and, in the age of social media and aggressive pharmaceutical compounding, that has become an ever-expanding wormhole of dangerous behavior.

The ballooning regulatory end-run is a frontal assault on intellectual property rights and patents which has serious systemic implications-such as slowing research into new and important uses for GLP-1 medicines. There is mounting evidence that these medicines may potentially treat a variety of other serious conditions, but to really dig into the scientific opportunities, the legitimate manufacturers of FDA-approved GLP-1 products will have to invest billions more into research and development. That is the good news.

The bad news is that if corporate compounders continue their dangerous exponential growth, manufacturers may be dissuaded from undertaking these additional high-risk research programs. It goes without saying that we should facilitate a system that encourages substantial investment into research and development by American pharmaceutical manufacturers that make potentially life- changing FDA-approved medicines under strict regulatory oversight to ensure patient safety.

As Otto von Bismarck said, "Only a fool learns from his own mistakes. The wise man learns from the mistakes of others."

References

1. FDA, New Drug Application (NDA) (Jan. 21, 2022), https://www.fda.gov/drugs/types-applications/new-drug-application-nda.
2. BIO, Clinical Development Success Rates and Contributing Factors, p. 3 (Feb. 2021), https://tinyurl.com/bp5mb3xy.
3. FDA, FDA's Concerns with Unapproved GLP-1 Drugs Used for Weight Loss (May 30, 2025), https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss.
4. 21 U.S.C. § 360(g)(1).
5. "503A" and "503B" refer to the applicable sections of the FDCA. 21 U.S.C. §§ 353a, 353b.
6. 21 U.S.C. §§ 353a(a).
7. 21 U.S.C. §§ 353a(a), (b)(1), (2).
8. FDA Center for Drug Evaluation and Research, Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food Drug, and Cosmetic Act, p. 5 (Jan. 2018), https://www.fda.gov/media/98973/download. There are reasons to doubt FDA's interpretation of section 503A as permitting compounding of a drug that is commercially available in the literal sense but in short supply. While that may be the subject of future reporting, it is not addressed here.
9. House of Representatives Conference Report No. 105-399, p. 94 (1997).
10. 21 U.S.C. § 353a(b)(3)(B).
11. FDA, Extension of the Period Before the Food and Drug Administration Intends to Begin Enforcing the Statutory 5 Percent Limit on Out-of-State Distribution of Compounded Human Drug Products, Docket FDA-2015-N-0030-8512 (Oct. 21, 2022), https://www.regulations.gov/document/FDA-2015-N-0030-8512.
12. 21 U.S.C. § 353b(a)(2).
13. 21 U.S.C. § 353b(b).
14. 21 U.S.C. § 353b(a).

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ISSN: 3067-6614 (Online)

15. 21 U.S.C. §§ 353b(a)(2)(A)(ii), (a)(5).

16. United States Department of Justice, Press Release (July 7, 2021), https://www.justice.gov/usao-ma/pr/former-owner-defunct-new-england-compounding-center-resentenced-14-years-prison.

17. While many of Section 503A's provisions has originally been added to the FDCA under a 1997 amendment, those provisions had gone unenforced after compounders filed a lawsuit that successfully invalidated the amendment due to its advertising provisions. Thompson v. Western States Medical Center, 535 U.S. 357 (2002).

18. Pew Charitable Trusts, U.S. Illness and Deaths Associated With Compounded or Repacked Medications, 2001–19, (Mar. 2020), https://www.pew.org/en/research-and-analysis/data-visualizations/2020/us-illnesses-and-deaths-associated-with-compounded-or-repackaged-medications-2001-19.

19. FDA, Compounding and the FDA: Questions and Answers, (Nov. 15, 2024), https://www.fda.gov/drugs/human-drug-compounding/ compounding-and-fda-questions-and-answers; FDA, FDA's Concerns with Unapproved GLP-1 Drugs Used for Weight Loss, (May 30, 2025), https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss.

20. Julian Gill, Empower Pharmacy says it sells 'quality' compounded drugs. 10 years of FDA violations raise doubts, Houston Chronicle, (May 12, 2025), https://www.houstonchronicle.com/news/investigations/article/empower-pharmacy-compounded-drugs-fda-20281795.php; Shelby Livingston, Drug Compounder Empower was built on risky shortcuts, ex-employees and inspections allege, Endpoints, (May 15, 2025), https://endpoints.news/pharmacy-empower-allegedly-used-low-quality-ingredients-skirted-rules/.

21. Julian Gill, Houston's Empower Pharmacy recalls 8,000 testosterone injections citing quality concerns, Houston Chronicle, (May 22, 2015), https://www.houstonchronicle.com/news/houston-texas/health/article/empower-pharmacy-testosterone-recall-20340925.php.

22. FDA, FDA warns patients and health care professionals not to use compounded drugs from Fullerton Wellness, (Nov. 1, 2024), https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-patients-and-health-care-professionals-not-use-compounded-drugs-fullerton-wellness.

23. Kenneth L. McCall, et al., Safety Analysis of compounded GLP-1 receptor agonists: a pharmacovigilance study using the FDA adverse event reporting system, (Apr. 29, 2025), https://www.tandfonline.com/doi/full/10.1080/14740338.2025.2499670?scroll=top&needAccess=true.

24. Dani Blum, More People Are Overdosing on Ozempic Alternatives, New York Times, (Aug. 6, 2024), https://www.nytimes.com/2024/08/06/well/ozempic-semaglutide-overdose-risks.html.

25. Brenda Goodman, Poison centers see nearly 1,500% increase in calls related to injected weight-loss drugs as people accidentally overdose, CNN, (Dec. 18, 2023), https://www.cnn.com/2023/12/13/health/semaglutide-overdoses-wellness; Diane Wilson, Testing online weight loss medications for potency—Here's what we found, ABC News (Nov. 28, 2024), https://abc11.com/post/how-lose-weight-abc-news-tests-potent- online-compounded-drugs-like-ozempic-wegovy-mounjaro-zepbound/15586570/.

26. 21 U.S.C. §§ 353a(b)(1), (2).

27. Patrick Wingrove & Dan Levine, Ozempic copies restricted after US judge denies injunction, Reuters, (Apr. 25, 2025), https://www.reuters.com/business/healthcare-pharmaceuticals/ozempic-copies-restricted-after-us-judge-denies-injunction-2025-04-24/.

28. FDA, FDA clarifies policies for compounders as national GLP-1 supply begins to stabilize (Apr. 28, 2025), https://www.fda.gov/drugs/drug-safety- and-availability/fda-clarifies-policies-compounders-national-glp-1-supply-begins-stabilize.

29. 21 U.S.C. § 353a(b)(2).

30. 21 U.S.C. §§ 381(a), (s).

31. Partnership for Safe Medicines, Knockoff Weight Loss Drugs From Illegal Foreign Sources, p. 11, https://www.safemedicines.org/wp-content/uploads/2019/09/PSM-White-Paper-v1-PUBLIC-VERSION.pdf.

32. Marta E. Wosinska, The Wild East of semaglutide, Brookings Institution, (Apr. 21, 2025), https://www.brookings.edu/articles/the-wild-east-of-semaglutide/.

33. Worthen DB. Good enough for America. Int J Pharm Compd. 2014 Jan-Feb;18(1):20-9, https://doi.org/10.26506/pharmhist.60.1-2.0017.

34. Partnership for Safe Medicines, Knockoff Weight Loss Drugs From Illegal Foreign Sources, p. 6-7, 13-14, https://www.safemedicines.org/wp-content/uploads/2019/09/PSM-White-Paper-v1-PUBLIC-VERSION.pdf.

35. FDA, Warning Letter—Synthetix Inc. DBA Helix Chemical Supply, MARCS-CMS 668918, (Feb. 7, 2024), https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/synthetix-inc-dba-helix-chemical-supply-668918-02072024; Marty Schladen, Pharmacy Board suspends another Ohio weight loss clinic's license, Ohio Capital Journal, (May 5, 2025), https://ohiocapitaljournal. com/2025/05/05/pharmacy-board-suspends-another-ohio-weight-loss-clinics-license/.

36. Partnership for Safe Medicines, Knockoff Weight Loss Drugs From Illegal Foreign Sources, p. 12-13, https://www.safemedicines.org/wp-content/uploads/2019/09/PSM-White-Paper-v1-PUBLIC-VERSION.pdf.

37. Berkeley Lovelace Jr., et al., Tennessee woman accused of selling fake weight loss drugs as counterfeit concerns grow, NBC News, (Dec. 17, 2024), https://www.nbcnews.com/health/health-news/tennessee-woman-accused-selling-fake-weight-loss-drugs-counterfeit-con-rcna184154.

38. Letter from Senator Thom Tillis to Attorney General Pam Bondi, FDA Commissioner Martin Makary, and DHS Secretary Kristi Noem, (June 5, 2025), https://www.tillis.senate.gov/services/files/54121424-5315-43C1-AF84-EC18A7550107; Letter from Senator Jim Banks to FDA Acting Commissioner Sara Brenner, (March 25, 2025), https://www.dropbox.com/scl/fi/jyj5g8ahgvi85qa5dndeh/03.26.25-Letter-to-Dr.-Brenner.pdf?rlkey=ujphw7gt1k17iqoi93cvpgtov&e=2&st=glsp2za4&dl=0.

39. Ashwin K. Chetty, et al., Online Advertising of Compounded Glucagon-Like Peptide-1 Receptor Agonists, JAMA Health Forum, (Jan. 17, 2025), https://jamanetwork.com/journals/jama-health-forum/fullarticle/2829225.

40. National Consumers League, The Influence of Disinformation on Attitudes and Beliefs About Compounded GLP-1 Drugs: A Dose of Reality, (May 2025), https://nclnet.org/wp-content/uploads/2025/05/The-Influence-of-Disinformation-on-Attitudes-and-Beliefs-About-Compounded-GLP-1- Drugs-Survey-Results.pdf.

41. Letter from Senators Richard Durbin and Roger Marshall to FDA Acting Commissioner Sara Brenner, (Feb. 7, 2025), https://www.marshall.senate.gov/wp-content/uploads/Durbin-Marshall_FDA-Letter_SB-DTC-Telehealth-Ad-output-FINAL-1.pdf.

42. 21 U.S.C. § 360(g)(1).

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